The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte HARALD MOHR and BERND LAMBRECHT

Appeal No. 2001-0400
Application No. 08/751,624

HEARD: August 9, 2001

Before WINTERS, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-16, 19-24, 26, and 27, all of the claims remaining in the application. At oral argument on August 9, 2001, Appellants' counsel Paula Morris (Reg. No. 31,516) expressly withdrew from appeal claims 23 and 26. Accordingly, the appeal with respect to claims 23 and 26 is dismissed.

Claims 1 and 16 are representative and read as follows:

1. A method for substantially completely inactivating viruses in a blood product, comprising:

providing a blood bag comprising a transparent wall retaining said blood product comprising said viruses;

adding to said blood bag a phenothiazine dye in an amount sufficient to produce a dye concentration in said blood product in the range of from about 0.5 µM to about 2 µM; and

irradiating said blood bag and said blood product comprising phenothiazine dye retained therein with visible light having a wavelength in the range of the absorption peak of said phenothiazine dye, wherein said irradiation passes through said transparent wall to said phenothiazine dye and continues for a period of time sufficient to substantially completely inactivate said viruses.

16. A method for removal of phenothiazine dye from a blood product, said method comprising passing said blood product over an adsorbing agent which strongly binds said phenothiazine and only weakly binds blood proteins, said adsorbing agent being selected from the group consisting of silica gel, polystyrene-divinylbenzene, acrylic ester polymers having a pore size in the range of from about 10Å to about 300 Å, and combinations thereof.

The examiner relies on the following references:

Hodgson et al. (Hodgson)	4,190,542	Feb. 26, 1980
Sugiyama et al. (Sugiyama)	4,728,432	Mar. 1, 1988

Bio-Rad Catalog, "Chromatographic Supports," Life Science Research Products, pp. 11-12 (1993)

Heinmets et al. (Heinmets), "Inactivation of Viruses in Plasma by Photosensitized Oxidation," Department of Defense Research Report, WRAIR-53-55, pp. 1-16 (1955)

Claims 1-3, 5-16, 19-22, 24, and 27 stand rejected under 35 U.S.C. § 112, first paragraph, as unsupported by an enabling disclosure.[1]

[1] The Examiner's Answer actually states that "[c]laims 1-3, 5-24, 26, 27 stand rejected under 35 U.S.C. § 112, first paragraph." However, claims 17 and 18 were cancelled in an amendment filed June 15, 1998 (Paper No. 9). This amendment was denied entry as an after-final amendment

Claims 1-15, 19-22, 24, and 27 stand rejected under 35 U.S.C. § 103 as obvious over Heinmets.

Claim 16 stands rejected under 35 U.S.C. § 103 as obvious over Heinmets in combination with either of Sugiyama or Hodgson, and Bio-Rad.

We reverse all of the rejections.

Background

Appellants' specification discloses a method for inactivating viruses in blood and blood products. In the disclosed method, a phenothiazine dye is added to the blood product and the dye-containing blood product is irradiated with visible light. See page 1. The specification states that

> phenothiazine dyes, particularly methylene blue (MB), neutral red, thionine, and toluidine blue (TB) are of special interest because they may, in combination with visible light, inactivate a number of viruses, including some viruses which do not possess a lipid envelope, e.g. adenovirus.

Page 3. The dye may be removed from the treated blood product using any of several adsorbing agents. Specification, pages 21-22.

Discussion

1. The nonenablement rejection

The claims are directed to a method of inactivating viruses in a blood product by adding a phenothiazine dye (at a final concentration of 0.5 µM to 2 µM) to a blood bag containing the blood product and irradiating with visible light.

(see the Advisory Action mailed June 18, 1998, Paper No. 11) but was entered after Appellants filed a request for a Continued Prosecution Application. See Paper No. 12, filed July 17, 1998, and the Office Action mailed August 6, 1998 (Paper No. 15). Thus, claims 17 and 18 are no longer pending. As noted above, the appeal of claims 23 and 26 has been dismissed.

The examiner rejected all of the claims except claim 4 (which is limited to using methylene blue as the dye) as nonenabled. The examiner reasoned that practicing the full scope of the claims "would require one of ordinary skill in this art undue experimentation to determine which dye would work in the instant invention." Examiner's Answer, page 9.

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). "[It] is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (1971).

In this case, the weight of the evidence in the record supports Appellants' position rather than the examiner's. The examiner sets out a Wands-based analysis. See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir.

1988). As part of that analysis, the examiner finds that "a large proportion" of phenothiazine dyes would be "inoperative" in the claimed process; that "the invention is complex and unpredictable," and that "the prior art indicates that most related dyes [i.e., related to methylene blue] are not effective for the claimed functions." See the Examiner's Answer, pages 9-10. The examiner, however, cites no evidence and provides no explanation for any of the findings that lead him to conclude that the claims are not enabled.

Appellants, on the other hand, cite several sources of evidence in the record as supporting enablement. See the Appeal Brief, pages 19-21, and the Reply Brief, page 2. First, the specification itself discloses use of six phenothiazine dyes to treat a blood product, and concludes that "[t]hionine (Th), azure A (AzA), azure C (AzC), and TB [toluidine blue] were of similar efficacy as MB [methylene blue]." See page 20. In addition, Appellants filed at least two declarations under 37 CFR § 1.132 that provide additional evidence of enablement. See declarations of Harald Mohr attached to Paper Numbers 7 and 9, filed Jan. 28, 1998, and June 10, 1998, respectively.[2]

In addition to the evidence cited by Appellants, we also note that Heinmets tested nine phenothiazine dyes for their effectiveness in inactivating viruses in plasma and found that all of them were at least somewhat effective. See Table 1

[2] Appellants also cite "the testimony of Dr. Mellors" as showing evidence of enablement. See the Appeal Brief, page 20. Appellants presumably refer to the declaration of John W. Mellors, which was submitted together with several other declarations on July 6, 1998 (attached to Paper No. 21). The Mellors declaration, however, was executed for submission with respect to a different patent application. It is unclear how Dr. Mellors's opinion—regarding the enablement of different claims by a different specification—would be relevant to the rejection of the present claims.

on page 6. In fact, Heinmets discloses that methylene blue, azure blue II, toluidine blue O, azure A, and azure B eliminated infectious virus upon irradiation,[3] while thionine, aniline blue, and azure C reduced but did not eliminate infectivity. See id.

All of these sources of evidence support enablement by showing that minimal experimentation would be required to practice the claimed method with many, if not most, phenothiazine dyes. The examiner has provided no evidence to rebut the evidence favoring enablement. We conclude that the examiner's position is not supported by a preponderance of the evidence in the record and therefore reverse the rejection for non-enablement.

2. The obviousness rejection based on Heinmets

The examiner rejected claims 1-15, 19-22, 24, and 27 under 35 U.S.C. § 103 as obvious in view of Heinmets. The examiner notes that Heinmets teaches inactivation of viruses in plasma using a combination of phenothiazine dye and irradiation. The examiner acknowledges that "the claims include the limitation of the concentration of dye is 0.5 – 2 micromolar whereas Heinmets teaches a concentration down to 10 micromolar for the same function in Table 1 and down to 0.5 micromolar in Table 3." Examiner's Answer, page 5. The examiner concludes that

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the same dyes as Heinmets for the same function at a selected low concentration because

[3] To be accurate, the Heinmets data show only that the treated plasma, when injected into mice, did not kill any of the mice. The actual number of infectious viral particles was not quantified.

> Heinmets teaches in Tables 1 and 3 how time of exposure is related to decrease in infectivity and one would have a high expectation of success in employing a lower concentration of dye with a longer time of exposure to achieve the same result.

Examiner's Answer, pages 5-6.

"In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art." In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992). "The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. Both the suggestion and expectation of success must be founded in the prior art, not in the applicant's disclosure." In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) (citations omitted).

"'Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so.' Although couched in terms of combining teachings found in the prior art, the same inquiry must be carried out in the context of a purported obvious 'modification' of the prior art. The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." Id. at 1266, 23 USPQ2d at 1783 (citations omitted, emphasis in original).

The examiner argues that those skilled in the art would have found it obvious to practice the claimed method, employing a dye concentration of 0.5 µM to 2 µM, in view of Heinmets. However, Heinmets consistently uses a dye

concentration of 10 µM for viral inactivation. The examiner cites Table 3 of Heinmets as showing practice of the disclosed method with dye concentrations as low as 0.5 µM, but we agree with Appellants that Table 3 would have led away from using dye concentrations of less than 2 µM. Table 3 shows that toluidine blue O at a concentration of 2.5 µM to 10 µM effectively inactivated Eastern equine encephalomyelitis virus in human plasma, but concentrations of 0.5 µM, 0.7 µM, and 1.0 µM did not. See Heinmets, page 8. Thus, Heinmets would have not have led those skilled in the art to modify the disclosed process in the manner recited in the instant claims.

The examiner provides no other evidence or reasoning that would have led those skilled in the art to modify the method disclosed by Heinmets by reducing the dye concentration to 0.5 µM to 2 µM. Since the relied-on reference does not provide motivation to modify the known process as required by the claims, the prior art does not support a prima facie case of obviousness. The rejection is reversed.

3. The obviousness rejection of claim 16

The examiner rejected claim 16 as obvious in view of the combined disclosures of Heinmets, either of Sugiyama or Hodgson, and the Bio-Rad catalog. Claim 16 is directed to a method for removing a phenothiazine dye from a blood product using a silica gel, polystyrene-divinylbenzene, or an acrylic ester polymer as an adsorbing agent.

The examiner noted that Heinmets teaches removal of a phenothiazine dye (toluidine blue) from blood using an ion exchange resin, but does not teach removal of such dyes using the claim-recited adsorbents. The examiner relies on either of Sugiyama or Hodgson to remedy this deficiency. The examiner reasons as follows:

> Sugiyama . . . teaches in the claims a method for removing soluble poisonous substances from blood by bringing the blood into contact with an absorbent which in claim 4 is activated carbon. In column 2 lines 40-48, the adsorbents may be porous resins, porous alumina, porous glass or ion exchange resins, selected depending upon the substances which are to be removed from blood by absorption.
>
> Hodgson . . . teaches a column for purifying blood, in column 2 lines 35-42, the column may be filled with granules having activated carbon or polystyrene granules. In column 2 lines 55-60, other polymers are shown. In column 4 line 6, any known particulate absorbent may be used.
>
> It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the macroporous polymeric beads of either Sugiyama or Hodgson in the method of Heinmets to remove selected substances from blood because Sugiyama and Hodgson show such porous polymers are compatible with blood and effectively remove selected substances.

Examiner's Answer, page 7.

"The PTO has the burden under section 103 to establish a prima facie case of obviousness. It can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988) (citations omitted). "The consistent criterion for determination of

obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. Both the suggestion and expectation of success must be founded in the prior art, not in the applicant's disclosure." In re Dow Chemical, 837 F.2d at 473, 5 USPQ2d at 1531.

The references relied on by the examiner in this case do not provide the required motivation to combine their teachings. Heinmets does not suggest using chromatographic media other than an ion exchange resin to remove a phenothiazine dye from treated plasma. Sugiyama and Hodgson, while they teach removing substances from blood using various adsorbents, do not discuss adsorption of a phenothiazine dye.

Sugiyama states that the object of his invention was "to remove soluble poison substances" from blood (column 2, line 13), which are defined as substances resulting from renal failure or liver failure, such as creatinine, uric acid, and urea. Column 1, lines 16-20. Sugiyama also teaches that the particular chromatographic medium used will depend on what substances are to be removed from the blood. Column 2, lines 43-45. Sugiyama does not discuss what media would be effective for removing a phenothiazine dye from blood.

Hodgson is directed to a method for removing "for instance, barbiturates or other poisons" from blood. Similar to Sugiyama, Hodgson provides no reason, suggestion, or motivation for using the disclosed process to remove a

phenothiazine dye from treated plasma. There is simply no adequate connection made in the cited references between the phenothiazine dye-containing blood taught by Heinmets and the chromatographic media taught by Sugiyama and Hodgson. the Bio-Rad catalog is not said to remedy, and does not remedy, this deficiency.

Since the prior art provides insufficient motivation to modify the process taught by Heinmets by substituting one of the claim-recited adsorbents for the ion exchange resin used by Heinmets, the prior art does not support a prima facie case of obviousness. We therefore reverse the § 103 rejection of claim 16.

Other Issues

During prosecution, Appellants submitted several declarations which had been executed for submission in application 08/707,992. That application bears no apparent formal relationship to the present application: neither application refers to the other, the priority applications in the two cases are completely different, and there is no overlap in inventive entity. The '992 application issued as U.S. Patent 5,827,644 on October 27, 1998, and seeks the benefit of an earlier filing date based on a chain of applications to at least May 11, 1989, and possibly October 28, 1988.

The disclosure and claims of the '664 patent concern inactivation of human immunodeficiency virus with a thiazine dye, such as methylene blue, and light. The '644 patent is prior art under 35 U.S.C. § 102(e) (assuming it is entitled

to benefit under 35 U.S.C. § 120). The '664 patent therefore appears to be relevant to the patentability of the instant claims.

Upon return of this case, the examiner should consider the effect of the '664 patent on the patentability of the instant claims.

Summary

We reverse the rejection for non-enablement because the examiner's position is not supported by a preponderance of the evidence. We reverse both of the obviousness rejections because the cited references do not provide the requisite motivation to modify their teachings in order to meet the limitations of the instant claims.

REVERSED

SHERMAN D. WINTERS Administrative Patent Judge	)
	) BOARD OF PATENT
DEMETRA J. MILLS Administrative Patent Judge	) APPEALS AND
	) INTERFERENCES
ERIC GRIMES Administrative Patent Judge	)

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